

REMARKS

Applicants respectfully request that the above application be reconsidered, as amended.

A. Claim Rejections Under 35 USC 112:

1. Examiner's Item 3. Claim 2 was rejected because the claim to a use of the product of Claim 1 did not include any steps involved in its use. Applicants have amended Claim 2 to provide for the step of administering the product.

2. Examiner's Item 4. Claim 7 was rejected under 35 USC 112, second paragraph, as indefinite for failing to point out and distinctly claim the subject matter regarded as the invention. The Applicants have replaced "an other" with -- another --.

3. Examiner's Item 5. Claim 13 was rejected under 35 USC 112, second paragraph, as indefinite for failing to point out and distinctly claim the subject matter regarded as the invention. The Applicants have amended "administrating" to -- administering --.

4. Examiner's Item 6 and 7. Claims 14 and 16-18 were rejected under 35 USC 112, first paragraph, for failing to comply with the enablement requirement. The Examiner states that the claims are drawn to a method of administering CCH-A with a hapten or protein. The Examiner stated "it is unclear whether any peptide or other protein will enhance the immunogenicity of any other peptide/protein simply by administering it along with CCH-A. Therefore, it does not enable one skilled in the art how to make or use the invention without undue experimentation." The Examiner then recounted the factors to be considered in determining whether undue experimentation is required, as they are summarized in *In re Wands*. The Examiner concludes that in the instant case, the quantity of experimentation would be large since there is a myriad of peptides to choose from, and that the amount of guidance is zero with regard to what peptides or other proteins might have enhanced immunogenicity when complexed to CCH-A.

Applicants respectfully traverse this rejection.

Applicants remind the Examiner that the criteria in *Wands* pertains to the making and using of the claimed invention. In the present case, the Applicants are not claiming “haptens and proteins” which have an enhanced immunogenicity when complexed with CCH-A. Rather, the Applicants are claiming a method for enhancing the immunogenicity of a hapten or a peptide, comprising the step of administering with the hapten or the peptide an amount of a product comprising a CCH-A subunit. The invention can be used when a researcher is interested in determining the immunogenic response to a particular antigen of interest, such as a hapten or a protein of interest. The method allows the researcher to enhance the native immunogenic response of the antigen by its coadministration with the CCH-A subunit. Applicants agree that it is practically impossible for Applicants to know the identity of every specific protein or hapten, or other antigen, that a particular researcher may be interested in studying for immunogenicity. That is not, however, the Applicants’ invention. Instead, Applicants have disclosed and claimed a definite method with which the researcher can enhance the immunogenicity of that antigen. Applicants have described and claimed a method that provides a definite step for enhancing the immunogenicity of an antigen of choice: co-administering the antigen with the CCH-A subunit.

Applicants respectfully request withdrawal of the rejection.

5. Examiner’s Item 8, 9 and 10. Claims 14 and 16-18 were rejected under 35 USC 112, first paragraph, for failing to comply with the written description requirement. The Examiner states that the claimed invention was not described in such a way as to reasonably convey to one skilled in the art that Applicants, at the time the application was filed, had possession of the claimed invention.

The Examiner stated “the claims are drawn to a method of use of an undefined genus of peptides and proteins.”

Applicants respectfully traverse the rejection.

The Applicants’ Claims 14 and 16-18 require the complexing of the proteins or peptides with the CCH-A subunit. The method claimed, which a person of ordinary skill would quickly understand, is that the complexing of the CCH-A subunit with a selected protein will enhance the immunogenic response of that protein. A person of ordinary skill would know that the Applicants have not claimed such proteins specifically. Rather, Applicants’ claimed invention relates to a method that uses the CCH-A subunit. The Examiner appears to focus on one aspect of the method that is admittedly broad: that is, the important breadth of the invention to assist researchers in improving the immunogenic response of a particular protein or antigen of interest.

The Examiner's emphasis of the *Vas-cath* case is misplaced. That case related to the support of claims provided by the drawings of the case. It nevertheless supports Applicants' position, since the Applicants are not claiming a particular peptide or protein, but is claiming a method for enhancing an antigen's immunogenic response by complexing it with the CCH-A subunit. This misunderstanding or misinterpretation of the case law is apparent in the Examiner's citation of *Fiers* and *Amgen*, which dealt with claims to a DNA molecule and to compounds and compositions, respectively.

Applicants respectfully request withdrawal of the rejection.

B. Claim Rejections Under 35 USC 102(b)

Examiner's Items 11, 12 and 13.

The Examiner cited the 2000-2001 Calbiochem catalog and Becker et al. as anticipating Claims 1 and 3-5 under 35 USC 102(b).

a. Calbiochem catalog: The Examiner states that this reference discloses CCH, and states that the composition is available in a sterile form, in a physiologically acceptable buffer that lacks magnesium or calcium, and contains the entire CCH protein (e.g, CCH-A and CCH-B).

b. Becker et al.: The Examiner states that this reference teaches various molecular weights of the individual CCH-A and CCH-B subunits, and that CCH has been successfully used as an immunogenic carrier protein. The Examiner asserts that the language of Claim 1 as filed includes "comprising" language, which can be anticipated by a reference disclosing a composition that contains CCH-A.

Applicants have amended Claim 1 to a product, and Claims 3-5 to a composition comprising a product, to require that the CCH-A protein is disassociated, and that the product consist essentially of the CCH-A subunit. In view of the amendments, Applicants contend that the claims are allowable over the cited art.

The Calbiochem catalog discloses a product containing a complete CCH protein, not a combination of disassociated proteins as required by the claims. Becker et al. disclosed that the CCH protein has been a successful carrier, and has two linked chains, the CCH-A and CCH-B subunits. Becker mentions the researchers' intentions to evaluate the immunotherapeutic activity of CCH, but does not disclose or suggest the specific activity of CCH-A, or the stability of the CCH-A subunit in the absence of Ca²⁺ and Mg²⁺ cations. Applicants are aware that the art has taught extensively that low molecular weight subunits of other hemocyanins have required the

presence of Ca^{+2} and Mg^{+2} . Such art references include *Marine tumor vaccine carriers: structure of the molluscan hemocyanins KLH and HtH*, Markl et al., J Cancer Res Clin Oncol (2001) 127 (Suppl 2): R3-R9, and *The Hemocyanin of the Squid Sepioteuthis lessoniana: Structural Comparison with Other Cephalopod Hemocyanins*, Chignell et al., Comp. Biochem. Physiol., Vol. 118B, No. 4, pp. 895-902 (1997). Applicants attach a copy of these references hereto for the Examiner's convenience.

Applicants wish to point out that the nomenclature of the specific subunits of CCH-A and CCH-B in Becker is incorrect. At the time of Becker, its author had named the 400-kDa species as CCH-B, and the small 350 kDa species as CCH-A. Since, the authors became aware that subunit hemocyanins of gastropods are to be named in ascending numeral or alphabetical order, beginning with the largest subunit.

C. Claim Rejections Under 35 USC 103(a)

Examiner's Items 14, 15 and 16.

The Examiner cited Linn et al. in view of Becker and the 2000-2001 Calbiochem catalog as making obvious Claims 6-20 under 35 USC 103(a). The Examiner states that Linn teaches the use of KLH as a successful immunogen carrier in the treatment of experimental bladder cancer, and the co-administration of a KLH with Immunocothel (a modified KLH) in the treatment of mice with bladder cancer. While not teaching the use of CCH, the Linn abstract and at page 6 are mentioned to point out that alternatives to KLH are being sought "to replace or supplement KLH", and that CCH "is a good option to supplement the use of KLH." The Examiner goes on to state that Becker teaches that KLH are potent immunostimulants, and that CCH belongs to this class of hemocyanins, and had been used as an immunogen carrier, and that the Calbiochem catalog notes CCH's used directly for hapten conjugation.

Applicants respectfully traverse the rejection, based on consideration of the amended claims, and the arguments that follow.

Applicants point out that the Linn reference specifically refers to the need to "replace or supplement" KLH, but only states that CCH would be a good option to supplement the use of KLH. Applicants contend that Linn does not disclose or suggest that CCH can be replaced by KLH. Furthermore, none of the references (Linn, Becker, or the Calbiochem catalog) disclose or suggest the use of a disassociated CCH subunit. Mere association of CCH with KLH as a related class of hemocyanins cannot render the claimed invention as obvious, particularly since Applicants' data clearly shows that the CCH protein and the CCH-B subunit provide

significantly lower immungenic responses compared to CCH-A (CCH:CCH-A of about 1:4, CCH-B:CCH-A of about 1:10). Consequently, Applicants' claim to the disassociated CCH-A subunit is nonobvious in view of the cited art.


D. Conclusion

It is believed that the above represents a complete response to the Examiner's rejections and places the application in condition for allowance. Accordingly, reconsideration and allowance of Claims 1-20 are respectfully requested.

Applicants would appreciate a telephone call should the Examiner have any questions or comments with respect to this response.

Respectfully submitted,

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